

REMARKS

Claims 1-12 are pending in the application. New claims 20-23 have been added to the application. Therefore, claims 1-12 and 20-23 are at issue.

New claim 20 recites that the compound is present in unit dosage composition as a free drug. Support for this amendment can be found in the specification at page 9, line 32 through page 10, line 3 and at page 7, lines 26-28. New claim 21 recites a unit dose of about 20 mg of the compound. Support for claim 21 can be found, for example, in claims 1-3. New claim 23 recites a unit dose of about 2 mg of the compound. Support for claim 23 can be found, for example, in Example 7 (e.g., at page 28, line 26, and in the Table entitled "IIEF Erectile Function Domain") which discloses a 2 mg dose of the compound. Support for new claim 22 can be found in claim 8.

Claims 1-12 stand rejected under 35 U.S.C. §112, second paragraph, because of a lack of antecedent basis for the term "form" in claim 1. Claims 1-12 have been amended to delete this term from the claims and improve the form of the claims. It is submitted that claims 1-12, and new claims 20-23, fully comply with 35 U.S.C. §112, second paragraph, and that the rejection should be withdrawn.

The examiner requested the identity of related applications in which double patenting may be an issue. In the parent application (U.S.S.N. 10/031,556), Emmick et al. U.S. Patent No. 6,451,807 was identified as such a related application.

Claims 1-12 stand rejected under 35 U.S.C. §102(b) as being anticipated by Daugan U.S. Patent No.

6,140,329 ('329). This rejection is based on the contention that the '329 patent discloses the compound recited in the claims in an individual dosage form containing the instant amount.

It has been recognized by the courts that a range which overlaps or lies inside a range disclosed by the prior art may be patentable. Further, as stated in the MPEP at §2131.03:

"II. < PRIOR ART WHICH TEACHES A RANGE WITHIN, OVERLAPPING, OR TOUCHING THE CLAIMED RANGE ANTICIPATES IF THE PRIOR ART RANGE DISCLOSES THE CLAIMED RANGE WITH 'SUFFICIENT SPECIFICITY'

When the prior art discloses a range which touches, overlaps or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with 'sufficient specificity to constitute an anticipation under the statute.' What constitutes a 'sufficient specificity' is fact dependent. If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with 'sufficient specificity' to constitute an anticipation of the claims."

For the reasons set forth below, applicants submit that the '329 patent does not anticipate the pending claims, because the subject matter of the pending claims is not disclosed in the '329 patent with

sufficient specificity to constitute an anticipation under the statute. In particular '329 patent fails to disclose dosages with any specificity as claimed in the present invention, where the present claims are directed to a unit dosage composition in much narrower range coupled with unexpected and surprising results associated with the claimed range.

The '329 patent discloses a broad range of dosages relating to a genus of compounds, including molecules identified as Compounds A and B. Compound A is the same molecule as Compound (I) disclosed in the present application. Specifically, the '329 patent discloses: "a compound of formula (I), and in particular compounds A and B will generally be in the range from 0.5-800 mg for an average adult patient (70kg). Thus, for a typical adult patient, individual tablets or capsules contain from 0.2-400 mg of active compound." ('329 patent, column 3, lines 48-55).

The present claims recite a pharmaceutical unit dosage composition suitable for oral administration, and containing an amount of compound (I) that is within the range of about 1 mg to about 20 mg. The dosage range of from about 1 mg to about 20 mg of compound (I) recited in the present claims is a much narrower range compared to the broad range disclosed in the '329 patent.

The surprising and unexpected results of the claimed invention is the criticality of a unit dosage composition of about 1 to about 20 mg of Compound (I), because this dosage range exhibits not only (i) low adverse side effects but also (ii) still being unexpectedly efficacious in treating sexual

dysfunction. As described below, the present patent application, and the attached declaration of Dr. Gregory D. Sides, teach unexpected results associated with a dosage range of from about 1 mg to about 20 mg of Compound (I). The surprising and unexpected results are that this dosage range causes low adverse side effects while remaining clinically effective in treating sexual dysfunction. These results are illustrated in the present specification. For example, Table IIEF (page 31) discloses the results of clinical studies that show the efficacy of Compound (I) at a dosing range of 2-100 mg. It is worth noting that the lower doses of Compound (I) were found to be efficacious.

The present specification also discloses that higher doses above 20 mg, although efficacious, result in an increased level of unpleasant adverse events (see page 32, lines 15-20). For example, the table in Example 7, at page 32 of the specification, clearly shows that undesirable adverse side effects, such as headache, dyspepsia, and back pain, increase with an increase in unit dosage (doses from 25 mg to 100 mg).

The present specification also cautions that "even though efficacy in the treatment of ED was observed at 25 mg to 100 mg unit doses, the adverse events observed from 25 mg to 100 mg dose must be considered," (page 32, lines 19-22)

Applicants submit that, taken together, the foregoing comments and results teach that a dose of Compound (I) below 25 mg possesses the unexpected and desirable property of effectively treating erectile dysfunction, while causing a substantially lower level

of adverse side effects compared to a dosage of compound I that is greater than 25 mg.

Additionally, with respect to a dosage of compound I in the range of about 1 mg to about 20 mg, submitted herewith as Attachment A is the declaration of Dr. Gregory D. Sides (hereafter referred to as the "Sides Declaration"), which was originally filed on January 15, 2004 in parent U.S.S.N. 10/031,556, now U.S. Patent No. 6,943,166.

In paragraph 8 of the declaration, Dr. Sides notes "the unexpected discovery of a unit dosage form incorporating about 1 to about 20 mg of Compound (I) that, when orally administered, effectively treats sexual dysfunction and substantially reduces various undesirable adverse events."

In paragraph 9 of the declaration, Dr. Sides states that "Example 7 shows that compound (I) is efficacious in the treatment of erectile dysfunction at 2 mg, 5 mg, and 10 mg dosages." In paragraph 10 of the declaration, Dr. Sides also notes that Example 7 "shows the unexpected decrease in treatment-emergent adverse events". Example 7 in parent U.S.S.N. 10/031,556 is identical to Example 7 in the present patent application.

In paragraph 10 of the declaration, Dr. Sides also describes the results of an analysis of pooled data from eight Phase 3 studies for placebo, 5 mg, 10 mg, and 20 mg doses of compound (I).

In paragraph 11 of the declaration, Dr. Sides states that "the data in paragraph 10 shows a dramatic reduction in adverse events associated with common adverse events, such as headache, dyspepsia and back

pain between the 20 mg and 50 mg dosages, and further reductions for the 5 mg and 10 mg dosages. This decrease of adverse events coupled with an efficacy across the claimed dose range is an unexpected advance in the art."

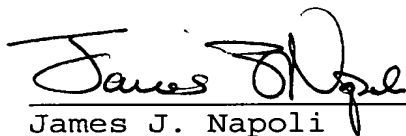
In view of the foregoing arguments and evidence, applicants submit that the '329 patent does not anticipate the pending claims, because the subject matter of the pending claims is not disclosed in the '329 patent with sufficient specificity to constitute an anticipation. Accordingly, applicants respectfully request that the rejection of Claims 1-12 under 35 U.S.C. §102(b) be withdrawn.

Should the examiner wish to discuss the foregoing, or any matter of form in an effort to advance this application toward allowance, the examiner is urged to telephone the undersigned at the indicated number.

Respectfully submitted,

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